IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	William BAXENDALE, *et al.*
Serial No:	10/527,767
Filing Date:	September 12, 2005
Title:	Chicken Astrovirus Type 2
Confirmation No:	5168
Group Art Unit:	1648
Examiner:	Hurt, Sharon L.
Attorney Ref:	2002.016 US

November 16, 2009

REPLY BRIEF under 37 C.F.R. 41.41

Mail Stop: Appeal
Board of Patent Appeals
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir/Madam:

In reply to the EXAMINER'S ANSWER sent September 17, 2009, Appellants ask the Board to consider the remarks that follow.

Appellants claim a subspecies of an astrovirus, not a new genus, as alleged by the Examiner. The genus is astrovirus, the species is chicken astrovirus and the subspecies, or subtype, is chicken astrovirus type 2. Appellants do not claim a nucleic acid sequence.

Appellants have deposited a reference strain and have described in detail the isolation and characterization of two additional isolates of the same claimed novel subtype.

"... [W]hat is adequate [[to] establish that the applicant was in possession of the claimed invention, including all the elements and limitations] depends upon the context of the claimed invention....We have articulated a variety of factors to evaluate the adequacy of the disclosure supporting "generic claims to biological subject matter." **Capon v. Eshhar,** 418 F. 3d 1349, at 1359 (Fed. Cir. 2005). These factors include "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the

science or technology, [and] the predictability of the aspect at issue." **Id.** **Ariad Pharma., Inc. v. Eli Lilly & Co.**, 560 F.3d 1366 (Fed. Cir. 2009).

Appellants have fulfilled these requirements. All of the procedures used by Appellants and all measured characteristics defining the subtype claimed are within the skill of the art.

"Astroviruses are small, round, non-enveloped, viruses with a typical diameter of 28-30 nm and harboring a positive stranded RNA genome. Astroviruses are distinct from other small round viruses (SRVs), such as parvoviruses, circoviruses, picornaviruses and caliciviruses, for example, in respect of their respective, characteristic morphological structures visible by electron microscopy." (Specification, page1, paragraph 3).

"The family of Astroviridae (*reference omitted*) is divided into two genera, i.e. mammalian astroviruses and avian astroviruses, the latter being extensively reviewed by Koci and Schultz-Cherry (*reference omitted).* In particular, this document reviews the characterizing genome organization and molecular biology of (avian) astroviruses and provides a sequence analysis of the astrovirus open reading frames." (Specification, page 1, paragraph 4).

"The present inventor has identified a new (sub)type of avian astrovirus isolateable from chickens (CAstV-2) that is immunologically distinct from the known chicken astrovirus ANV (CAstV-1) and from other avian astroviruses." (Specification, page 2, paragraph 1).

"A CAstV-2 according to the invention can be obtained from the Depository Institute (CNCM of the Institute Pasteur) or can be isolated from infected animals in the field and can be identified as such by reaction with specific antisera raised against the deposited virus in an immunological assay as described in the Examples." (Specification, page 2, lines 12-15).

Methods for preparing "appropriate antiserum" raised against live CAstV and inactivated CAstV are provided in paragraphs 1 and 2 on page 3 of the Specification.

"Preferably, the present invention provides a chicken astrovirus type 2 (CAstV-2), characterized in that the virus is the CAstV deposited under accession no. I-2932... or an immunological[ly] related CAstV that has a percent relatedness (%R) with the deposited virus of at least 32, more preferably at least 50, most preferably at least 70 as determined by cross-neutralization and calculated according to the method of Archetti and Horsefall (*reference omitted).* 'R-values' of 32-50 between a test virus and the deposited CAstV

indicate a clear immunological relationship between the two, whereas a 'R-value' of 50-70 and at least 70 indicate minor or little/no immunological difference, respectively." (Specification, page 3, paragraph 4).

Appellants defined the CAstV-2 subtype by its chemical, physical and immunological characteristics.

"**Treatment with ether and IDUR:** The virus is a stable agent resistant to ether and its growth was not inhibited by IDUR – indicating it is a RNA virus." (Specification, page 3, lines 2-30).

"**Immunofluorescence test:** Infected cell cultures when tested using the immunofluorescent test show cytoplasmic fluorescence with no nuclear fluorescence. High antibody titre serum could be used at a dilution of >1:256 giving bright fluorescence." (Specification, page 4, lines 1-4). A minimum of 32 defines the subtype in the claims and in the examples. (Specification, page 14).

"**Cross neutralization test:** In a plaque reduction test the virus is neutralized well with antiserum induced against itself with serum titres greater than 512 often observed. Antisera against the following agents [nine different avian viruses are listed] have shown no cross neutralization." (Specification, page 4, paragraph 2). A minimum of 128 defines the subtype in the claims and in the examples. (Specification, page 14).

"**Electron microscopy:** Suspension containing viral particles purified from infected cells was placed on carbon-coated copper grids and subjected to negative staining. Examination in an electron microscope revealed the presence of clusters of small-round viruses with a diameter ranging from 25-30 nm." (Specification, page 4, paragraph 3).

"**RT-PCR and Sequence determination: ...**total RNA was isolated from purified virus... For an RT-PCR, two primers derived from a conserved region situated in ORF1 of small-round-structured virus (SRSV) genomes...were employed. ...The putative amino acid sequences derived from the PCR product were identified as having moderate similarities to the non-structural proteins of [four different types of astroviruses]. This genetic information indicated that the agent is chicken astrovirus belonging to the family *Astroviridae*." (Specification, page 4, paragraph 4).

In Example 1 three different CAstV-2 isolates were isolated from chickens. The VDU/As1 CAstV-2 isolate was obtained from tracheal swabs taken from 10 symptomatic broiler chicks and plaque purified. The VDU/As2 CAstV-2 isolate, which ultimately was the deposited reference strain, was obtained from white blood cells taken from

symptomatic broiler chicks and identified by the astrovirus induced cytopathic effect observed in two of the chick embryo liver (CEL) cell tissue cultures inoculated with the white blood cells. The VDU/As3 CAstV-2 isolate was obtained from a pool of homogenized small intestines from symptomatic chicks by culturing on CEL cells followed by plaque purification. (Specification, pages 8 and 9).

In Example 2 production of antiserum to VDU/AS2 (the deposited reference CAstV-2) is described in detail, as are the virus neutralization assay, the immunofluorescence test and the gel diffusion test. (Specification, pages 9-11).

In Table 1a the immunological relationships between VDU/AS2 (CAstV-2) and ANV (CAstV-1), and VDU/AS2 (CAstV-2) and TastV/ TEV (turkey astrovirus) are reported. In Table 1b the immunological relationships between a different isolate,VDU/AS1 (CAstV-2) and ANV (CAstV-1), and VDU/AS1 and DVH-2 (duck astrovirus) are reported. The results illustrate numerically that there is essentially no immunological relationship with these other viruses, not even with the other subspecies of chicken astrovirus, ANV, which is an isolate of CAstV-1. VDU/AS2 and VDU/AS1 produced neutralization titers of 256 and 1600, and Immunofluorescence titers of 128 and 256, with themselves, respectively, compared with <16 and <10 for both tests for the other astroviruses, even CAstV-1. (Specification, pages 12 and 13).

The three isolates of CAstV-2 isolated from infected chicks by Appellants, by contrast, showed a high degree of immunological similarity, as reported in Table 2, using antisera raised against the three individual isolates of CAstV-2. The cross neutralization titres among VDU/AS1, VDU/AS2 and VDU/AS3 ranged from 128 to 512. The immunofluorescence titers for antisera raised against the other CAstV-2 isolates ranged from 32 to 64. All three CAstV-2 isolates reacted positively in the gel diffusion assay. These results are the basis for the defining minimum neutralization (128) and immunofliorescence (32) limitations in Appellants' independent claim to the new subtype, chicken astrovirus type 2 (CAstV-2). (Specification, page 14).

The requirements for demonstrating possession of the invention are set forth in **Ariad Pharma.,Inc. v. Eli Lilly & Co.,** 560 F. 3d 1366 (Fed. Cir. 2009), quoting several earlier decisions. " "To satisfy the written description requirement, ' the applicant does not have to utilize any particular form of disclosure to describe the subject matter claimed, but the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.' 'In other words, the applicant must 'convey with

reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention,' and demonstrate that by disclosure in the specification of the patent." **Carnegie Mellon Univ. v. Hoffman La Roche Inc.,** 541 F.3d 1115,1122 (Fed. Cir. 2008) (quoting **In re Alton** , 76 F.3d 1168, 1172 (Fed. Cir. 1996). ""Whether the description requirement is satisfied is a fact-based inquiry that will depend on the nature of the claimed invention and the knowledge of one skilled in the art at the time an invention is made and a patent application filed."" **Carnegie Mellon** , 541 F. 3d at 1122.

Appellants have discovered a novel subtype of a chicken astrovirus and have deposited an isolate as the reference strain. They have disclosed in detail how to obtain a virus from symptomatic chickens and identify a virus so obtained as an astrovirus. They have disclosed in detail how to determine if the isolate is the type 2 (CAstV-2) chicken astrovirus subtype using methods described in the Specification, providing specific neutralization, immunofluorescence and gel diffusion assays and numerical values to be met using antiserum raised against the deposited reference isolate for an isolate to be a type 2 astrovirus according to the invention. Further, they have provided the results from assessing two additional isolates obtained by Appellants from chickens that were determined by the experimental methods described in the present application to be additional examples of the novel chicken astrovirus type-2. It cannot be sustained that Appellants did not have the claimed invention in hand at the time the application was filed.

The Examiner has stated, "[t]o provide written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of a genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof." (Examiner's Answer).

Those of ordinary skill in the art, which inherently presumes a high level of skill in the biological arts, can through ordinary procedures isolate virus from symptomatic chickens and plaque purify a specimen, as described in Appellants' examples. They can, using ordinary methods, determine that the virus isolated is an astrovirus. Then, by preparing antiserum using the deposited reference isolate, again using methods known to the ordinary practitioner, as well as described in the Specification, they can assess whether the newly isolated astrovirus is a member of the CAstV-2 subtype by testing, using

procedures both known to the ordinary practitioner and described in the Specification, to determine if the minimum neutralization and immunofluorescence titers are met. If so, the new isolate is a member of the type 2 subtype, just as are the two representative isolates found by Appellants and described in the Specification using the same assays.

Appellants have more than met the Examiner's requirements of "physical and/or chemical properties," such as, for example, treatment with ether and IDUR to show the virus is a RNA virus, electron microscopy to show it is a small-round virus with a diameter ranging from 25-30 nm, and PCR determination that the subject is an astrovirus.

Appellants have provided functional characteristics through neutralization and immunofluorescence assay requirements based on the deposited reference virus isolate, which also qualify as meeting the structure/function correlation, as immunological results depend on structure.

Appellants have further provided "methods of making," i.e., methods of extracting, purifying, categorizing (as astrovirus), and assaying for subtype 2, sufficient for any skilled practitioner to obtain chicken astrovirus type 2.

The Examiner has dismissed the two additional isolates of the claimed subtype described by Appellants in the Specification because "Appellants' disclosure does not describe or provide DNA sequences for these isolates."

Appellants submit that DNA sequences are not required to demonstrate that Appellants had the invention as claimed in hand at the time the application was filed. The two examples of the subtype, in addition to the deposited reference isolate, are described in the Specification from their acquisition from symptomatic (and the symptoms are described) chicks, through testing to determine that they were astroviruses and then assaying to determine whether they met the immunological criteria required to categorize them as members of the type 2 subtype. The ordinary practitioner reading the Specification knows and understands that Appellants had CAstV-2 in hand. The rejection under 35 U.S.C. 112, first paragraph, for not having possession of the claimed invention must be reversed.

Appellants do not believe that any other fee is due in connection with this filing. If, however, Appellants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No.19-0365. In addition, if there is ever any other fee deficiency or overpayment in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or credit such overpayment to Deposit Account No.19-0365.

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Appellants submit that the pending claims are in condition for allowance and request the rejections in the August 6, 2008, final Office action be reversed, and claims 1 and 4-10 be allowed.

Respectfully submitted,

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